

HORST LINDHOFER et al.

PATENT

Application No.: 09/094,921, Group Art Unit: 1642, Examiner: Holleran, A.

Amendment No. 3 -- Page 5

72 human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-  
73 [CH2]-human-IgG3\*-[CH3]  
74 human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-  
75 [CH2]-human-IgG3\*-[CH3]  
76 rat/mouse.

C2 1 20. (twice amended) Method according to claim 1, in which said bispecific antibodies are  
2 added in an amount of 2 to 100 µg.

#### REMARKS

The recitations added to claim 1 are taken from claim 22, now deleted. No new matter is presented. Entry of this amendment and reconsideration of the application are respectfully requested.

Respectfully submitted,



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**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

1. (twice amended) Method for the preparation of a vaccine for immunization of humans and animals against tumor cells comprising the steps of:
  - a) isolating autologous tumor cells;
  - b) treating the tumor cells to prevent the survival thereof following reinfusion;
  - c) incubating the thus treated tumor cells with intact heterologous bispecific [~~and/or~~  
~~trisp~~pecific] antibodies showing the following properties:
    - $\alpha$  - binding to a T cell;
    - $\beta$  - binding to at least one antigen on a tumor cell;
    - $\gamma$  - binding, by their Fc portion [~~(in the case of bispecific antibodies), or by a third~~  
~~specificity (in the case of trisp~~pecific antibodies)] to Fc receptor-positive cells **capable of activating the Fc receptor-positive cell whereby the expression of cytokines, co-stimulatory antigens or both is induced or increased,** wherein the bispecific antibodies are members selected from the group consisting of the following isotype combinations:
      - rat-IgG2b/human-IgG1,
      - rat-IgG2b/human-IgG2,
      - rat-IgG2b/human-IgG3[oriental allotype G3m(st) = binding to protein A],
      - rat-IgG2b/human-IgG4;
      - rat-IgG2b/rat-IgG2c;
      - mouse-IgG2a/human-IgG3[caucasian allotypes G3m(b+g) = no binding to protein A, in the following indicated as \*]
      - mouse-IgG2a/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2a/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2a/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-[VH-CH1,VL-CL]-human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2: > aa position 251]-human-IgG3\*[CH3]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge-CH2-CH3]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG2-[hinge-CH2-CH3]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG3-[hinge-CH2-CH3, oriental allotype]

rat-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG4-[hinge-CH2-CH3]

human-IgG1/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG2[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG2/human-[VH-CH1,VL-CL]-human-IgG2-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG3\*-[CH2-CH3]

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4[N-terminal region of CH2]-human-IgG3\*[C-terminal region of CH2 : > aa position 251]-human-IgG3\*[CH3]

mouse-IgG2b/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2b/human-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-IgG2b/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG3\*-[CH2-CH3]

mouse-[VH-CH1,VL-CL]-human-IgG4/rat-[VH-CH1,VL-CL]-human-IgG4-  
[hinge]-human-IgG4-[CH2]-human-IgG3\*-[CH3]

human-IgG1/rat-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-[CH2]-  
human-IgG3\*-[CH3]

human-IgG1/mouse-[VH-CH1,VL-CL]-human-IgG1-[hinge]-human-IgG4-  
[CH2]-human-IgG3\*-[CH3]

human-IgG4/human-[VH-CH1,VL-CL]-human-IgG4-[hinge]-human-IgG4-  
[CH2]-human-IgG3\*-[CH3]

rat/mouse.

20. (twice amended) Method according to claim 1, in which said bispecific [or trispecific] antibodies are added in an amount of 2 to 100 µg.